

CLAIMS

1. A method of forming particles, comprising:
accelerating a first stream comprising a first liquid;
applying a charging voltage of at most 1.5 kV to the first stream;
5 and
vibrating the first stream, to form particles.
2. The method of claim 1, further comprising solidifying the particles.
3. The method of claim 1, wherein the first liquid comprises a
hydrophilic polymer.
- 10 4. The method of claim 3, wherein the first liquid comprises one or
more polymers selected from the group consisting of chitosan, gelatin, alginate,
carboxy methyl cellulose, dextran, hydroxypropyl cellulose, poly(acrylamide),
poly(acrylic acid), poly(allylamine) hydrochloride,
poly(diallyldimethylammonium chloride), poly(N,N-dimethyl acrylamide),
15 poly(ethylene glycol), poly(ethylene oxide), poly(maltotriose), poly(methacrylic
acid), poly(N-isopropyl acrylamide), poly(propylene glycol), poly(styrene
carboxylic acid), poly(styrene sulphononic acid), poly(styrene sulphonate),
poly(vinyl acetate), poly(vinyl alcohol), poly(vinyl butyral), poly(2-vinyl-N-
methyl pyridinium iodide), poly(4-vinyl-N-methyl pyridinium), poly(2-vinyl
20 pyridine), poly(2-vinyl pyridinium bromide), poly(vinyl pyrrolidone), p(methyl
vinyl ether), hydroxyalkyl starch, alkylcellulose, hydroxyalkylcellulose,
hydroxyarylcellulose, and copolymers thereof.
5. The method of claim 3, wherein the particles comprise a
pharmaceutical composition.
- 25 6. The method of claim 3, wherein the particles comprise a core and a
shell.

7. The method of claim 6, wherein the particles comprise a plurality of shells.

8. The method of claim 7, wherein the core comprises a pharmaceutical composition.

5 9. The method of claim 3, wherein the accelerating comprises contacting the first stream with a second stream, and the second stream comprises a second liquid.

10. The method of claim 9, wherein the second stream surrounds the first stream.

10 11. The method of claim 3, further comprising forming the first stream by passing the first liquid through a nozzle.

12. The method of claim 11, wherein the nozzle has a diameter greater than 1/2 of the average diameter of the particles.

15 13. The method of claim 11, wherein the nozzle has a diameter at least equal to the average diameter of the particles.

14. The method of claim 3, wherein the particles have an average diameter of at least 10 nm to at most 100 μm .

20 15. The method of claim 3, wherein the particles have an average diameter of at least 50 μm to at most 100 μm , and 90% of the particles have a diameter that is within 2% of an average diameter of the particles.

16. The method of claim 3, wherein the particles have an average diameter of at least 1 μm to at most 50 μm , and 90% of the particles have a diameter that is within 1 μm of an average diameter of the particles.

25 17. The method of claim 3, wherein the accelerating is a step for accelerating the first stream, and

the vibrating is a step for vibrating the first stream.

18. The method of claim 3, wherein solidifying comprises:
heating the particles to a temperature of at least 90 °C and of at most
170 °C.

5 19. The method of claim 2, wherein the solidifying comprises:
heating the particles to a temperature of at least 125 °C and of at
most 135 °C.

20. The method of claim 2, wherein the solidifying comprises:
maintaining the particles at a pressure of at least 0.1 mm Hg and of
10 at most 760 mm Hg, while heating the particles to a temperature within ± 50 °C of
the boiling point of water at the pressure.

21. The method of claim 2, wherein solidifying comprises:
cooling the particles to a temperature of -10 °C to 25 °C.

15 22. The method of claim 2, wherein solidifying comprises:
cooling the particles to a temperature of -2 °C to 6 °C.

23. The method of claim 3, further comprising:
treating the particles with a crosslinking agent.

20 24. The method of claim 23, wherein the crosslinking agent is selected
from the group consisting of: formaldehyde, glyceraldehyde, glutaraldehyde,
dextran dialdehyde, ethylene glycol, di(ethylene glycol), polyethylene glycol,
propylene glycol, di(propylene) glycol, polypropylene glycol, ethylene glycol
dimethacrylate, di(ethylene glycol) dimethacrylate, poly(ethylene glycol)
dimethacrylate, poly(lauryl methacrylate-co-ethylene glycol dimethacrylate),
propylene glycol dimethacrylate, di(propylene glycol) dimethacrylate,
25 poly(propylene glycol) dimethacrylate, malonic dihydrazide, ethylmalonic
dihydrazide, succinic dihydrazide, glutaric dihydrazide, adipic dihydrazide,
isophthalic dihydrazide, oxalyl dihydrazide, pimelic dihydrazide, 3,3'-

sulfonyldibenzenesulfonic dihydrazide, m-xylylene isocyanate, 4-methyl-m-phenylene diisocyanate, 2-methyl-m-phenylene diisocyanate, 3,3'-dimethoxy-4,4'-biphenylene diisocyanate, 4-Br-6-methyl-1,3-phenylene diisocyanate, 4-Cl-6-methyl-1,3-phenylene diisocyanate, toluene 2,4-diisocyanate, 1,3-phenylene diisocyanate, 1,4-phenylene diisocyanate, 2,4,6-trimethyl-1,3-phenylene diisocyanate, 1,4-diisocyanatebutane, 1,6-diisocyanatehexane, 1,8-diisocyanateoctane, isophorone diisocyanate; carbodiimides such as N,N-(3-dimethylaminopropyl)-N-ethyl carbodiimide, CaCl_2 , divinylsulfone, sulfonylurea, hydrolysable polyrotaxane, L-lysine methyl ester, and genipin.

- 10 25. A method of forming chitosan or alginate particles, comprising:
accelerating a first stream comprising a solution of chitosan or
alginate,
applying a charging voltage of at most 1.5 kV to the first stream;
vibrating the first stream, to form particles; and
15 maintaining the particles at a pressure of at least 0.1 mm Hg and of
at most 760 mm Hg, while heating the particles to a temperature within ± 50 °C of
the boiling point of water at the pressure;
wherein the accelerating comprises contacting the first stream with a
second stream, and the second stream comprises a hydrophobic liquid.
- 20 26. The method of claim 25, further comprising solidifying the
particles.
27. The method of claim 25, wherein the particles comprise a
pharmaceutical composition.
28. The method of claim 25, wherein the accelerating comprises
25 contacting the first stream with a second stream, and
the second stream comprises a second liquid.
29. The method of claim 25, further comprising forming the first stream
by passing the first liquid through a nozzle.

30. The method of claim 29, wherein the nozzle has a diameter greater than 1/2 of the average diameter of the particles.

31. The method of claim 31, wherein the particles have an average diameter of at least 10 nm to at most 100 μm .

5 32. Particles comprising chitosan or alginate having an average diameter of at least 1 μm to at most 100 μm , wherein 90% of the particles have a diameter that is within 1 μm of an average diameter of the particles.

33. The particles of claim 32, wherein the particles comprise a pharmaceutical composition.

10 34. The particles of claim 32, wherein the particles comprise a core and a shell.

35. The particles of claim 34, wherein the core comprises a pharmaceutical composition.

15 36. The particles of claim 32, wherein the particles comprise a plurality of shells.

37. A method of forming gelatin particles, comprising:
accelerating a first stream comprising an aqueous solution of gelatin,
applying a charging voltage of at most 1.5 kV to the first stream;
20 vibrating the first stream, to form particles; and
subjecting the particles to a temperature at most 10 $^{\circ}\text{C}$ above the gelling temperature of the solution of gelatin;
wherein the accelerating comprises contacting the first stream with a second stream, and the second stream comprises a hydrophobic liquid.

25 38. The method of claim 37, further comprising:
collecting the particles in a collection bath comprising a surfactant.

39. The method of claim 37, further comprising:
treating the particles with a crosslinking agent.

40. The method of claim 39, wherein the crosslinking agent is selected from the group consisting of: formaldehyde, glyceraldehyde, glutaraldehyde, dextran dialdehyde, ethylene glycol, di(ethylene glycol), polyethylene glycol, propylene glycol, di(propylene) glycol, polypropylene glycol, ethylene glycol dimethacrylate, di(ethylene glycol) dimethacrylate, poly(ethylene glycol) dimethacrylate, poly(lauryl methacrylate-co-ethylene glycol dimethacrylate), propylene glycol dimethacrylate, di(propylene glycol) dimethacrylate, poly(propylene glycol) dimethacrylate, malonic dihydrazide, ethylmalonic dihydrazide, succinic dihydrazide, glutaric dihydrazide, adipic dihydrazide, isophthalic dihydrazide, oxalyl dihydrazide, pimelic dihydrazide, 3,3'-sulfonyldibenzenesulfonic dihydrazide, m-xylylene isocyanate, 4-methyl-m-phenylene diisocyanate, 2-methyl-m-phenylene diisocyanate, 3,3'-dimethoxy-4,4'-biphenylene diisocyanate, 4-Br-6-methyl-1,3-phenylene diisocyanate, 4-Cl-6-methyl-1,3-phenylene diisocyanate, toluene 2,4-diisocyanate, 1,3-phenylene diisocyanate, 1,4-phenylene diisocyanate, 2,4,6-trimethyl-1,3-phenylene diisocyanate, 1,4-diisocyanatebutane, 1,6-diisocyanatehexane, 1,8-diisocyanateoctane, isophorone diisocyanate; carbodiimides such as N,N-(3-dimethylaminopropyl)-N-ethyl carbodiimide, CaCl_2 , divinylsulfone, sulfonylurea, hydrolysable polyrotaxane, L-lysine methyl ester, and genipin.

41. The method of claim 1, further comprising chopping the particles.